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Final Submittal**1-(4-Chlorophenyl)-4,4-dimethyl-3-pentanone****CAS # 66346-01-8****Revised HPV Test plan****Bayer CropScience LP****January 2008****Executive Summary**

Bayer CropScience LP (Bayer) hereby provides the final submittal for 1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone (CAS# 66346-01-8) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program. This submission completes Bayer's commitment to CAS # 66346-01-8 under the HPV Program.

IUPAC Name	Common Name	CAS#
1-(4-chlorophenyl)-4,4-dimethyl-3-pentanone	HWG alkylketone	66346-01-8

HWG alkylketone is used as an intermediate in the production of an agricultural fungicide.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of high concern for aquatic toxicity, low - moderate concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and low concern for acute mammalian toxicity. This substance is produced as a closed-system intermediate.

Data Review

Physicochemical properties:

The properties of HWG alkylketone were available from internal studies, except for the Partition Coefficient which was calculated with EPIWin Modeling Program. HWG alkylketone is liquid at ambient temperatures and has a boiling point of approximately 270 °C. Vapor pressure is less than 0.001 hPa at 20°C. The calculated octanol/water partition coefficient is 3.97 and it is slightly soluble in water (20.7 mg/l at 20°C). Data are available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

Photodegradation of HWG alkylketone was calculated at a 16.5 hours half-life. Fugacity modeling demonstrates partitioning to the soil (72.5%) and water (22.3%) compartments. Biodegradation modeling demonstrates that HWG alkylketone is not readily biodegradable. No water stability study has been located. Based on similar compounds and experience, this compound is expected to be extremely stable in water (>1 year at pH 5–9). Although this material is not readily biodegradable, it is not considered to be bioaccumulative. Data are available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

Several aquatic studies have been conducted. LC50 results of 4.9 mg/l (96 hr, *Leuciscus idus*) and 3.74 mg/l (96 hr, *Salmo gairdneri*); and an EC50 of 3.2 mg/l (48 hr, *Daphnia*) were determined. The 96 hour EC50 value for growth rate of *Pseudokirchneriella subcapitata* (ErC50) is 3.3 mg/L; the cumulative biomass EbC50 is 2.5 mg/L. HWG alkylketone is toxic to aquatic organisms. Data are available for all endpoints; no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Toxicity studies in animals show that HWG alkylketone is of low acute toxicity by all routes of exposure: oral LD50 = 4748 mg/kg (rat); inhalation LC50 > 2928 mg/m³ (rat); and dermal LD50 > 5000 mg/kg (rat).

HWG alkylketone was negative for gene mutations in a bacterial mutagenicity test. HWG alkylketone was negative in an “*in vivo* Mammalian Erythrocyte Micronucleus Test” (OECD 474).

An OECD TG 422, repeated dose toxicity study with screening reproductive and developmental toxicity endpoints was conducted. Groups of 12 rats/sex were treated with 0 (vehicle), 15, 80 and 400 mg Folicur alkylketone/kg body weight/day by oral gavage. The NOAEL for systemic toxicity was 80 mg/kg bw/d. There were no effects on fertility or developmental effects at 400 mg/kg bw/d, the highest dose tested. Slight declines in both male and female pup weight and pup weight gain were observed in the 400 mg/kg/day group. Effects on the pups are considered to be secondary to the toxicity observed in the females at this same dose level.

Data are available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

“Beyond SIDS” Endpoints:

Studies have been performed to investigate skin and eye irritation. HWG alkylketone was found to be non-irritating to the skin and eyes of rabbits. (See Table 2 and IUCLID document).

Exposure considerations

Since this chemical is used as a closed-system intermediate, there is limited exposure potential to humans, aquatic organisms and the environment. Workers use protective equipment in any situation where accidental exposure is possible. There is no intentional disposal to a wastewater system. With controls imposed, exposure is negligible.

Conclusion

Existing data indicate that this chemical is of high concern for aquatic toxicity, low - moderate concern as Persistent Organic Pollutants (POP), low concern for skin irritation, and low concern for acute mammalian toxicity. All endpoints have been fulfilled and no additional testing is needed. This submission completes Bayer's commitment to CAS # 66346-01-8 under the HPV Program.

Table 1. Available data for HWG ALKYLKETONE

Endpoint	HWG ALKYLKETONE (CAS# 66346-01-8)
Physical-Chemical Data	
Molecular weight	224.73
Physical state	liquid
Melting Point	18 °C
Boiling Point	270 °C
Vapour Pressure	< 0.001 hPa @ 20 °C
Partition Coefficient (logPow)	3.97
Water Solubility	20.7 mg/L @ 20 °C
Environmental Fate	
Photodegradation	T _½ = 16.5 hours
Fugacity (distribution)	Air – 1.16 % Water – 22.3% Soil – 72.5% Sediment – 3.99%
Biodegradability	T _½ > 1 year
Water Stability	> 1 year at pH 5-9
Ecotoxicology	
Acute Fish Toxicity 96 hrs LC50	4.9 mg/L (<i>Leuciscus idus</i>) 3.74 mg/L (<i>Salmo gairdneri</i>)
Acute Invertebrate Toxicity 24 hrs LC50	3.2 mg/L (<i>Daphnia magna</i>)
Algal Toxicity 96 hr EC50	ErC50= 3.3 mg/L; EbC50 = 2.5 mg/L (<i>Pseudokirchneriella subcapitata</i>)
Mammalian Toxicology	
Acute Toxicity	LD50 = 4748 mg/kg bw (oral, male/female rats) LC50 > 2938 mg/m ³ (inhalation, 4 hr, male/female rats) LD50 > 5000 mg/kg bw (dermal, male/female rats)
Mutagenicity	Ames = negative
Mammalian Micronucleus (<i>in vivo</i>)	Negative
Repeated Dose Toxicity	NOAEL = 80 mg/kg bw
Reproductive Toxicity	NOAEL = 400 mg/kg bw
Developmental Toxicity	NOAEL = 400 mg/kg bw

* Robust summaries and References can be found in the IUCLID document.

Table 2. “Beyond SIDS” data for HWG ALKYLKETONE

Endpoint	HWG ALKYLKETONE (CAS# 66346-01-8)
Skin Irritation	Not irritating (4 hrs, rabbit)
Eye Irritation	Not irritating (24 hrs, rabbit)

* Robust summaries and References can be found in the IUCLID document.

Table 3. Data Availability for HWG ALKYLKETONE

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	No
Boiling Point	✓	✓	No
Vapour Pressure	✓	✓	No
Partition Coefficient (logPow)	✓	✓	No
Water Solubility	✓	✓	No
Environmental Fate			
Photodegradation	✓	✓	No
Fugacity	✓	✓	No
Biodegradability	✓	✓	No
Water Stability	✓	✓	No
Ecotoxicology			
Acute Fish Toxicity	✓	✓	No
Acute Invertebrate Toxicity	✓	✓	No
Algal Toxicity	✓	✓	No
Mammalian Toxicology			
Acute Toxicity	✓	✓	No
Mutagenicity	✓	✓	No
Chromosome Aberration	✓	✓	No
Repeated Dose Toxicity	✓	✓	No
Reproductive Toxicity	✓	✓	No
Developmental Toxicity	✓	✓	No

✓ = data available and considered adequate.